Newly Developed Embolic Material Mesosphere and Titanium

Experimental and Clinical Studies

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Introduction

To date, various particulate embolic materials have been developed and investigated experimentally, but none have reached a stage where they are permanently suitable for routine clinical application.

The particles should have a non-absorbable character and good biocompatibility. ES particles (ES; BioSphere Medical, MA) fulfill these general requirements. The particles should be spherical so that they can be sorted into various sizes by sieving, providing uniformly graded and calibrated material. Spherical particles provide geometrically optimal occlusion of the vascular lumen.

They are hydrophilic, non-absorbable, collagen-coated, acrylic microspheres. Distal portions of the microvasculature can be reached by the microspheres. PVA particles have been the most commonly used for embolization [5]. Embolization experiments were independently conducted in an animal model using a combination of ES. However, this embolic material is not radiopaque. We thought that combining it with titanium could solve this problem. Pure titanium is radiolucency material. Before clinical use, we investigated ES experimental study using combination with titanium. In this paper, we report the clinical application of ES compared with PVA in the embolization of meningiomas.

Animal Experimental Study

The femoral artery of a pig (approximately body weight: 20 kg) was catheterized with a 5F catheter under general anesthesia. Imaging was performed to guide the insertion of the catheter (5F) to the renal artery and using a micro-catheter (Transit II: J&J Cordis. Japan) and micro-guide wire (Boston scientific; Trancent 0.014), ES (250 – 350 μ) was injected and embolization was performed. Embolism of the renal artery was confirmed by angiograms. The radiopaque material that was used in the embolization could not be mixed with the pure titanium granules (150 μ), although it could be delivered, it was likely to cause incomplete blockade of the delivery catheter. Fluoroscopy indicated that titanium was likely to cause embolism of the proximal artery (figure 2). But it is not yet used for embolic material.

Findings of Pathological Examination

On the macroscopic findings, the proximal renal artery was found to be completely obliterated by titanium granules. On the contrary, ES was found to consider causing sufficient embolism in the distal side more than titanium, which will be especially important in neoplasm (figure 2). On the high power findings ES did not lead to thrombosis in larger vessels. But ES completely obliterates precapillary vessels.

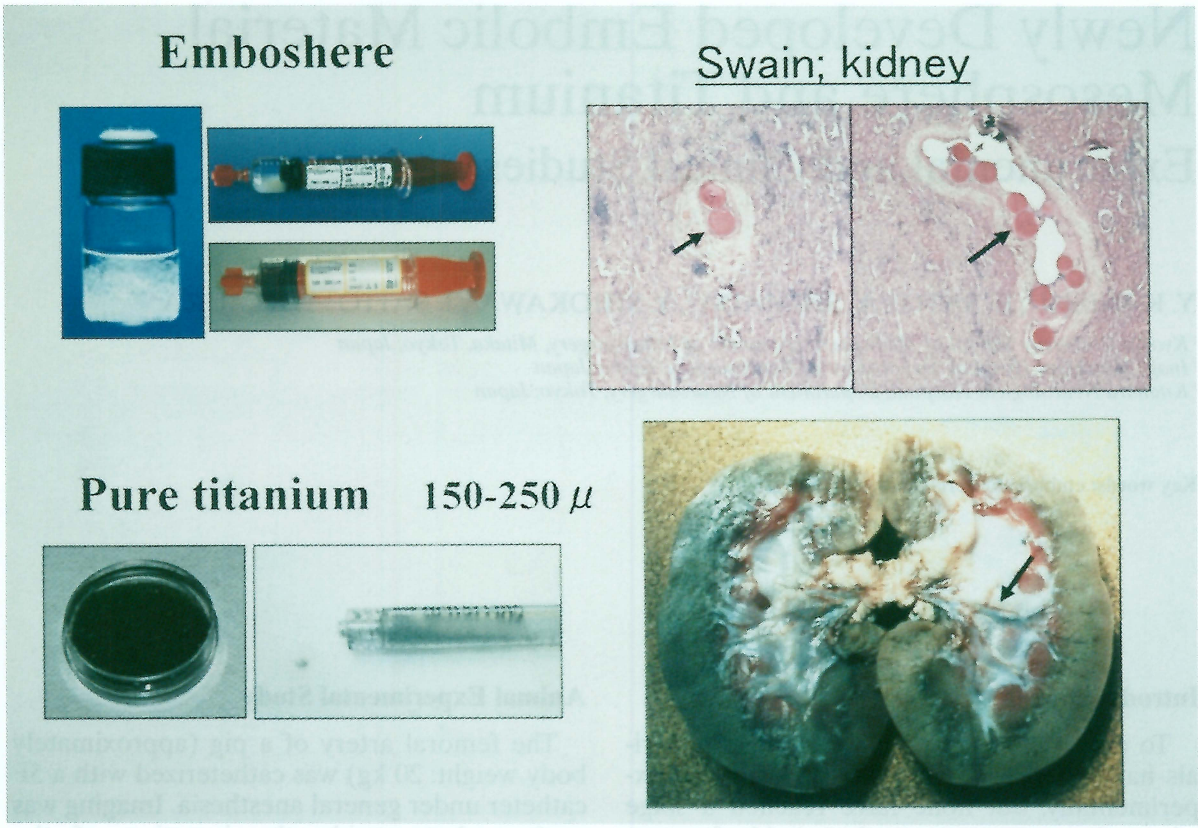

Figure 1 Embosphere and pure titanium. Pathological investigation after embolization to a renal artery of pig. Upper - There are Embospheres in the periphery of the artery. Lower - there is titanium powder in the proximal end of the artery.

Clinical Cases

The clinical trial was performed in three patients with meningiomas. First, we explained to patient and family the material's safety and necessity of embolization and finally derived obtained an informed consent. They were all convexity meningiomas. In one case, ES embolized the middle meningial artery. In other two cases, PVA was used as .embolization material. The meningioma was totally removed by surgical excision one to three days after embolization with PVA. When the influence of PVA and ES embolization were pathologically compared, PVA was not found within the tumor and it embolized proximal arteries. On the other hand ES was found to penetrate the tumor more distal (figures 3, 4).

Discussion

ES are hydrophilic particles; they are porous with a spherical globular form and can be wet-sieved through calibrated sieves to adjust particle size distribution. A particle consists of an acrylic polymer-copolymer (trisacryl). ES results in a soft and elastically deformable character that enables the temporary deformation of the particles when they are injected through a microcatheter with an inner diameter slightly smaller than that of the particles. The acrylic polymer gelatin microspheres were commercially available. However, this embolic material is radiolucency. We thought that this problem could be resolved by combining it with titanium.

Usage of titanium in medicine includes aneurysmal clips, instruments and prosthetics; it is well known to have a satisfactory biocompatibility. Titanium is a low dense, as low as 4.5 g/cm^3, so its mechanical burden to a patient is small when it is inside of the body. Furthermore, titanium is a radiopaque material. Powder of pure titanium was a size ranges (150 - 250 microns), as determined from animal experiment's model, but it was difficult to pour. The necessity of adding titanium needs to further consideration. If like ES, titanium turns out to be a useful embolic material in animal experimental models and then useful in the clinical use, it can be considered to be superior to PVA. However, if the use of titanium alone remains equivocal in these settings it may still be found to be useful in combination with ES.

ES have the following advantages: flexibility and elasticity, non-aggregating, uniform occlusion, and predictable penetration. It's elasticity and hydrophilic surface prevent aggregation of ES particles within the catheter, simplifying its handling and facilitating its accurate delivery to target vessels. On the other hand, PVA has the following disadvantages: irregular shape, clumping non-uniform occlusion and more proximal occlusion. In addition to these disadvantages, PVA is radiolucent material like ES.

Therefore, pure titanium powder, currently accepted as a biocompatible substance, was used in the experiments reported here. In the future, combination of titanium with ES will be considered.

Laurent[2] first reported the use of ES for embolization in 1996. Spies[4] clinically applied this material for the treatment of leiomyoma, and Bendszus1 compared ES with PVA in the preoperative treatment of meningiomas. PVA was found to enter a neoplasm when particles had a size of 45 – 150 microns or less, wearers ES had 150 to 250 microns. The ES

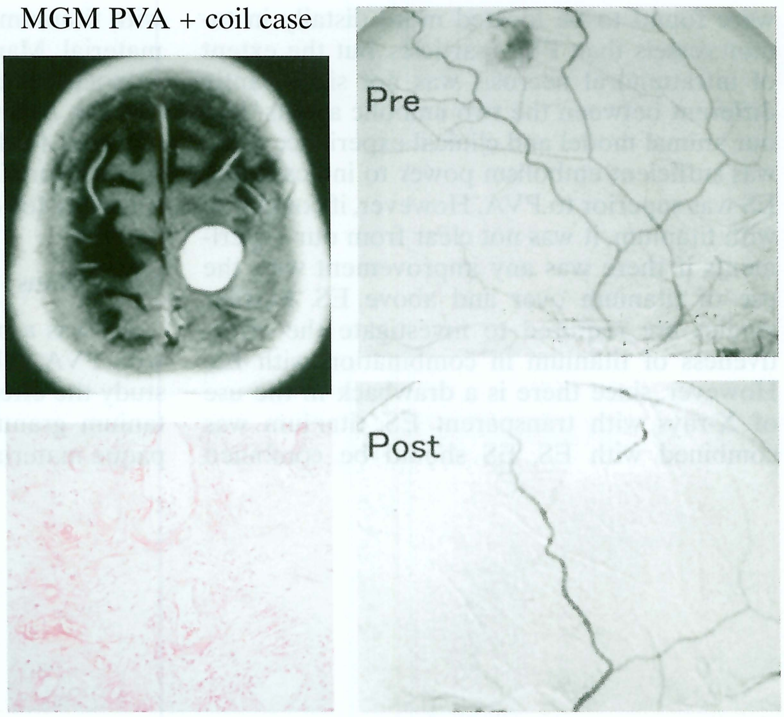

Figure 2 Clinical case: Meningioma; embolization using by PVA and small coil. MRI showed a well-demarcated mass. Pre-angiograms showed a 'sun-burst' phenomenon. Post-embolization angiograms showed complete embolization. Pathological findings demonstrated proximal occlusion by PVA.

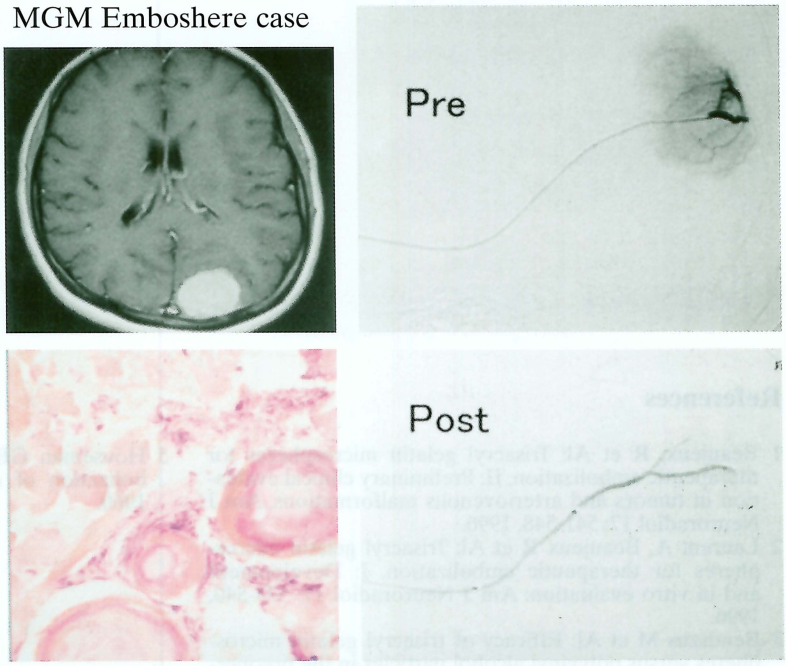

Figure 3 Clinical case: Meningioma; embolism using Embospheres. MRI showed a well-demarcated mass. Pre-angiograms showed a 'sun-burst' phenomenon. Post-embolization angiograms showed a complete embolization. Pathological findings showed that there are more Embospheres in the more peripheral artery compared with the PVA cases.

were found to be located more distally in tumor vessels than PVA particles, but the extent of intratumoral necrosis was not significantly different between the two embolic agents [1,3]. In our animal model and clinical experience there was sufficient embolism power to indicate that ES was superior to PVA. However, if compared with titanium, it was not clear from our experiments if there was any improvement with the use of titanium over and above ES. Further studies are required to investigate the effectiveness of titanium in combination with ES. However, since there is a drawback in the use of X-rays with transparent ES, titanium was combined with ES. ES should be combined with titanium to develop a more ideal embolic material. Many new substances have been developed and applied to cerebrovascular surgery. At this point, further experiments are required to determine their characteristics, especially for clinical use, before they can be used routinely for embolization.

Conclusions

ES was a better embolic material compared with PVA. Although it is necessary to further study the effectiveness of ES combined with titanium granules has the advantage of radiopaque material.

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